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      18 MAY 23
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                 The Analysis Edition of STN Express with Discover!
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      20 JUN 13
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                 and text labels
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FILE LAST UPDATED:

19 JUL 2005

<20050719/UP>

MOST RECENT UPDATE WEEK:

200528 <200528/EW>

FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

=> s HIP1 or (huntingtin () interacting protein)

31 HIP1

405 HUNTINGTIN

6 HUNTINGTINS

406 HUNTINGTIN

(HUNTINGTIN OR HUNTINGTINS)

34642 INTERACTING

122116 PROTEIN

103067 PROTEINS

134770 PROTEIN

(PROTEIN OR PROTEINS)

3697 INTERACTING PROTEIN

(INTERACTING (W) PROTEIN)

104 HUNTINGTIN (W) INTERACTING PROTEIN

L1 122 HIP1 OR (HUNTINGTIN (W) INTERACTING PROTEIN)

=> s prostate or colon

21247 PROSTATE

381 PROSTATES

21261 PROSTATE

(PROSTATE OR PROSTATES)

24121 COLON

508 COLONS

1601 COLA

25865 COLON

(COLON OR COLONS OR COLA)

L2 34409 PROSTATE OR COLON

=> s 12 and 11

L3 80 L2 AND L1

=> s genes/ti

L4 2913 GENES/TI

=> s 13 and 14

L5 6 L3 AND L4

=> s williams/au

=> s 16 and 15

L7 1 L6 AND L5

=> d ibib

L7 ANSWER 1 OF 1

ACCESSION NUMBER: TITLE (ENGLISH): TITLE (FRENCH): PCTFULL COPYRIGHT 2005 Univentio on STN

2000018916 PCTFULL ED 20020515

HUMAN GENES AND GENE EXPRESSION PRODUCTS GENES HUMAINS ET PRODUITS D'EXPRESSION

GENIQUE

INVENTOR(S):

WILLIAMS, Lewis, T.; ESCOBEDO, Jaime; INNIS, Michael, A.; GARCIA, Pablo, Dominguez; SUDDUTH-KLINGER, Julie; REINHARD, Christoph;

GIESE, Klaus; RANDAZZO, Filippo; KENNEDY, Giulia, C.;

POT, David; KASSAM, Altaf; LAMSON, George; DRMANAC, Radoje; CRKVENJAKOV, Radomir;

DICKSON, Mark;
DRMANAC, Snezana;
LABAT, Ivan;
LESHKOWITZ, Dena;
KITA, David;
GARCIA, Veronica;
JONES, Lee, William;
STACHE-CRAIN, Birgit

PATENT ASSIGNEE(S):

CHIRON CORPORATION;

HYSEQ INC. English

LANGUAGE OF PUBL.:

DOCUMENT TYPE:

Patent

PATENT INFORMATION:

DESIGNATED STATES

W:

AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE

SN TD TG

APPLICATION INFO.: PRIORITY INFO.:

WO 1999-US22226 A 19990923 US 1998-60/102,161 19980928 US 1998-60/102,180 19980928 US 1998-60/102,380 19980929 US 1998-60/103,815 19981008 US 1998-60/105,877 19981027

=> d kwic

L7 ANSWER 1 OF 1 PCTFULL COPYRIGHT 2005 Univentio on STN TIEN HUMAN GENES AND GENE EXPRESSION PRODUCTS

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TIFR
       GENES HUMAINS ET PRODUITS D'EXPRESSION GENIQUE
IN
      WILLIAMS, Lewis, T.;
       ESCOBEDO, Jaime;
       INNIS, Michael, A.;
       GARCIA, Pablo, Dominguez;
       SUDDUTH-KLINGER, Julie;
       REINHARD, Christoph;
       GIESE, Klaus;
       RANDAZZO, Filippo;
       KENNEDY, Giulia, C.;
       POT, David;
       KASSAM, Altaf;
       LAMSON, George;
       DRMANAC, Radoje;
       CRKVENJAKOV, Radomir;
       DICKSON, Mark;
       DRMANAC, Snezana;
       LABAT,. .
DETD
       The invention features polynucleotides that are expressed in human
       tissue, specifically
       human colon, breast, and/or lung tissue. Novel nucleic acid
       compositions of the invention of
       particular interest comprise a sequence set forth in any. . .
       generating the cDNA. Where the provided
       I 0 polynucleotides are isolated from cDNA libraries, the libraries are
       prepared from mRNA of human
         colon cells, more preferably, human colon cancer
       cells., even more preferably, from a highly
       metastatic colon cell, Km 12L4-A.
       sample, or any normal
       tissue of the patient, especially those that express the
       poiynucleotide-related gene of interest (e.g.,
       brain, thymus, testis, heart, prostate, placenta, spleen,
       small intestine, skeletal muscle, pancreas, and
       the mucosal lining of the colon). A difference between the
       polynucleotide-related gene, mRNA, or
       protein in the two tissues which are compared, for example in molecular
       weight,.
       a test sample obtained from a patient suspected of having or being
       susceptible to a disease
       (e.g., breast cancer, lung cancer, colon cancer and/or
       metastatic forms thereof), and comparing the
       detected levels to those levels found in non-nal cells (e.g., cells
       substantially unaffected.
       of breast cancer), lung cancer
       (e.g., small cell carcinoma, non-small cell carcinoma, mesothelioma, and
       other forms and/or stages of
       lung cancer), and colon cancer (e.g., adenomatous polyp,
       colorectal carcinoma, and other forms
       and/or stages of colon cancer).
       polynucleotide is differentially expressed across various cancer types.
       Thus,
       for example, expression of a polymicleotide that has clinical
       implications for metastatic colon cancer
       can also have clinical implications for stomach cancer or endometrial
       cancer.
```

Detection of **colon** cancer. The polynucieotides of the invention exhibiting the appropriate expression pattern can be used to detect **colon** cancer in a subject. Colorectal cancer is one of the 1 5 most common neoplasms in humans and perhaps the most.

the levels of expression.

colorectal cancer. Colorectal cancer begins as polyps, which are small, benign growths of cells that form on the inner lining of the colon. Over a period of several years, some of these polyps accumulate additional mutations and become cancerous. Multiple familial colorectal cancer disorders have been identified, which are summarized as follows: 1) Familial adenomatous polyposis (FAP); 2) Gardner's syndrome; 3) Hereditary nonpolyposis colon cancer (HNPCC), - and 4) Familial colorectal cancer in Ashkenazi Jews. The expression of appropriate polynucleotides of the invention can be used in the diagnosis, prognosis and management of colorectai cancer. Detection of colon cancer can be determined using expression levels of any of these sequences alone or in combination with

Determination of the aggressive nature and/or the metastatic potential of a colon cancer can be determined by comparing levels of one or more polynucleotides of the invention and comparing total levels of another sequence. . . Nat Genet. (I 994) 4(3):217; Fearon ER, Ann N YAcad Sci. (I 995) 768: 1 0 1). For example, development of colon cancer can be detected by examining the ratio of any of the polynucleotides of the invention to the levels of oncogenes. . .

FAP or p53). Thus expression of specific marker polynucleotides can be used to discriminate between normal and cancerous colon tissue, to discriminate between colon cancers with different cells of origin, to discriminate between colon cancers with different potential metastatic rates, etc.

3 5 Detection of **prostate** cancer. The polynucleotides and their corresponding genes and gene
3 8
products exhibiting the appropriate differential expression pattern can be used to detect **prostate**cancer in a subject. Over 95% of primary **prostate** cancers are adenocarcinomas. Signs and symptoms may include: frequent urination, especially at night, inability to urinate, trouble starting or holding back urination, . . .

Many of the signs and symptoms of **prostate** cancer can be caused by a variety of other non-cancerous conditions. For example, one common cause of many of these signs and symptoms is a condition called benign prostatic hypertrophy, or BPH. In BPH, the **prostate** gets bigger and may block the flow or urine or interfere with sexual function. The methods and compositions of the invention can be used to distinguish between **prostate** cancer and such non-cancerous conditions.

```
invention can be used in conjunction with conventional methods of
diagnosis,
e.g., digital rectal exam and/or detection of the level of
prostate specific antigen (PSA), a substance
produced and secreted by the prostate.
1: Source of Biological Materials and Overview of Novel Polynucleotides
Expressed b
the Biological Materials
cDNA libraries were constructed from either human colon cancer
cell line Km 12L4-A
(Morikawa, et al., CancerResearch (1988) 48:6863), KM12C (Morikawa et
al. CancerRes. (1988)
48:1943-1948), or MDA-MB-231 (Brinkley et.
2L49 KM I 2L4-A. etc.) are wel 1-recognized in the art as a model cell
line for the study of colon
cancer (see, e.g., Moriakawa et aL, supra; Radinsky et aL Clin. Cancer
Res. (I 995) 1:19; Yeatman et
I 0 aL, (I. . .
Table 4. Description of cDNA Libraries
Library Description Number of
(lib Clones in
Library
I Human Colon Cell Line Km 12 L4: High Metastatic 308731
Potential (derived from Km 12C)
2 Human Colon Cell Line Km 12C: Low Metastatic 284771
3 Human Breast Cancer Cell Line MDA-MB-23 1: High 326937
Metastatic Potential; micro-mets in lung
4. . bFGF 42100
TREATED (PCR (OligodT) cDNA library)
14 Human microvascular endothelial cells (HMVEQ - 42825
VEGF TREATED (PCR (OligodT) cDNA library)
1 5 Normal Colon - UC#2 Patient (MICRODISSECTED PCR 282722
(OligodT) cDNA library)
16 Colon Tumor - UC#2 Patient (MICRODISSECTED PCR 298831
(OligodT) cDNA library)
1 7 Liver Metastasis from Colon Tumor of UC#2 Patient 303467
(MICRODISSECTED PCR (OligodT) cDNA library)
18 Normal Colon - UC#3 Patient (MICRODISSECTED PCR 36216
(OligodT) cDNA library)
19 Colon Tumor - UC#3 Patient (MICRODISSECTED PCR 41388
(OligodT) cDNA library)
20 Liver Metastasis from Colon Tumor of UC#3 Patient 30956
(MICRODISSECTED PCR (OligodT) cDNA library)
21 GRRpz Cells derived from normal prostate epithelium 164801
22 WOca Cells derived from Gleason Grade 4 prostate 162088
cancer epithelium
23 Normal Lung Epithelium of Patient # 1 006 306198
(MICRODISSECTED PCR (OligodT) cDNA library)
Primary tumor, Large Cell Carcinoma of.
Donna M. Peehl, Department of Medicine, Stanford University School of
Medicine. GRRpz was
derived from normal prostate epithelium. The WOca cell line is
a Gleason Grade 4 cell line.
inhibitin gthe activity of the encoded gene
```

product would serve to inhibit tumor cell angiogenesis. Detection of

expression of these sequences

in colon cancer tissue can be valuable in determining diagnostic, prognostic and/or treatment information associated with the prevention of achieving the malignant state. . Example 8: High Metastatic Potential Colon Cancer Versus Low Metastatic Colon Cancer Cells Table 8 summarizes polynucleotides that represent genes differentially expressed between high metastatic potential and low metastatic potential colon cancer cells. Table 8. Low metastatic potential colon (lib2) > high metastatic potential colon cancer cells (lib I) SEQ ED NO: ILibl Clones ILib2Clones ILib2/Libl I 157 8 i 8.67 1103 i 0 6 16.5 16.5 i 189]o Example 9: High Tumor Potential Colon Tissue Vs. Metastasized Colon Cancer Tissue The following table summarizes polynucleotides that represent genes differentially expressed between high tumor potential colon cancer cels and cells derived from high metastatic potential colon cancer cells of a patient. Table 9. High tumor potential colon tissue (lib 1 6) vs. high metastatic colon tissue (lib 1 7) SEQ ED NO: I Lib 16 Clones Lib 17 Clones ILibl 100 io 6.89 I 3 112 370 3.94 134 Low Met Colon (lib2) > High Met Colon (lib 1) 67 134 High Met Breast (lib3) > Low Met Breast (Lib4) 85 1209 Low Met Lung (lib9) > High Met Lung (lib8) 17.44 1209 'Colon Tumor Tissue (libl6) > Normal Colon Tissue (libI 5) 3.42 209 Colon Tumor Tissue (lib 19) > Normal Colon Tissue (lib 1 8) 5 209 High Met Colon Tissue (lib20) > Normal Colon Tissue (lib 1 8) 1209 Colon Tumor Tissue (lib I 9) > High Met Colon Tissue (lib20) 74 1316 High Met Colon (lib 1) > Low Met Colon (lib2) i316 Low Met Breast (1ib4) > High Met Breast (Lib3) 17.28 645 Low Met Breast (lib4) > High Met Breast. toward a metastatic phenotype. For example, SEQ ID NO: 209 corresponds to a gene that is expressed at relatively higher levels in colon tumor tissue than in high metastatic potential colon tumor tissue, and at relatively higher levels in high metastatic potential colon tumor tissue than in normal colon tissue. Thus a relatively increased level of expression of the gene corresponding to SEQ ID NO: 209 may be used as marker of a pre-metastatic

colon cells either alone

or in combination with other markers.

genome IE-35
490 JABO16492.1 Homo sapiens hJTB gene, complete cds e-I 18
491 X98176 H.sapiens mRNA for MACH-beta- I protein IE-36
Homo sapiens huntingtin interacting protein
HYPK mRNA,
492 AF049613 partial cds 7E-22
493 AF039690.1, HomosapiensantigenNY-CO-8 (NY-CO-8) mRNA, partialeds IE-37
INM-001003IHomo sapiens ribosomal protein, large, PI ribosomal
494 phosphoprotein PI mRNA, complete cds. 4E-3. . .

WEST Search History

Hide Items | Restore | Clear | Cancel

DATE: Wednesday, July 20, 2005

Hide? Set Name Query H				
DB=PGPB,USPT,EPAB; PLUR=YES; OP=OR				
	L34	127 and probe	1	
	L33	127 and complementary	0	
	L32	6316272.pn.	1	
	L31	L30 not @ay>2001	19	
	L30	11 and (prostate or colon)	33	
	L29	L28 not @ay>2001	19	
	L28	l3 and (prostate or colon)	33	
	L27	6794501.pn.	1	
	L26	6794501.pn	0	
	L25	L24 and 11	0	
	L24	colorectal.ti.	198	
	L23	L22 and (prostate or colon)	0	
	L22	6235879 pn.	1	
	L21	L20 and L14	2	
	L20	L19 and L12	3	
	L19	(ross or mizukami or Rao).in.	20409	
	L18	L2 and L12	5	
	L17	L13 and (prostate or colon)	2	
	L16	L15 and (prostate or colon)	2	
	Ŀ15	L13 and L14	2	
	L14	L2.clm.	34430	
	L13	L3 and L12	5	
	L12	L7 or L8 or L10	7	
	L11	L7 or L8 or L10L10	4	
	L10	Ll.ab.	6	
	L9	L1.ab. L8	7	
	L8	Ll.ti.	3	
	L7	L1.clm.	3	
	L6	L5 and (screen\$ or detect\$ or determin\$ or diagnos\$)	30	
	L5	L3 and L4	30	
	L4	= 2001	5469895	

L3	L1 and L2	58
L2	cancer\$ or neoplas\$ or angiogen\$ or tumor\$	170265
L1	hip1 or (huntington adj interacting adj protein)	69

END OF SEARCH HISTORY

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FILE 'CANCERLIT' ENTERED AT 08:12:12 ON 20 JUL 2005
L1 29 S HIP1 OR (HUNTINGTIN () INTERACTING PROTEIN)
       1221530 S CANCER? OR TUMOR? OR NEOPLAS?
L2
        44388 S PROSTAT OR COLON
L3
       158156 S PROSTAT? OR COLON?
L4 .
          3 S L4 AND L1
L5
    FILE 'MEDLINE' ENTERED AT 08:14:55 ON 20 JUL 2005
          124 S HIP1 OR (HUNTINGTIN () INTERACTING PROTEIN)
L6
L7
       1726468 S CANCER? OR TUMOR? OR NEOPLAS?
L8
       161221 S PROSTATE OR COLON
L9
            3 S L8 AND L6
     FILE 'CAPLUS' ENTERED AT 08:15:52 ON 20 JUL 2005
L10 176 S HIP1 OR (HUNTINGTIN () INTERACTING PROTEIN)
L11
         89631 S PROSTATE OR COLON
        17 S L10 AND L11
L12
L13 2474250 S SCREEN? OR IDENTIF? OR DETECT?
L14 1134526 S EXPRESS?
            15 S L14 AND L12
L15
            12 S L15 AND L13
L16
            0 S L16 NOT PY>2001
L17
L18
            0 S L17 NOT PY>2002
            0 S L16 NOT PY>2002
L19
     FILE 'PCTFULL' ENTERED AT 08:18:19 ON 20 JUL 2005
    122 S HIP1 OR (HUNTINGTIN () INTERACTING PROTEIN)
L20
L21
         34409 S PROSTATE OR COLON
         87552 S CANCER? OR TUMOR? OR NEOPLAS?
L22
         113 S L22 AND L20
L23
L24
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            7 S L24 NOT PY>2000
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L26
            80 S L20 AND L21
L27 7 S L26 NOT PY>2000
L28 386911 S SCREEN? OR DETECT? OR DIAGNOS?
       79 S L28 AND L26
L29
L30 .
            5 S L20/AB
            1 S L30 AND L21
L31
           14 S L20/CLM
L32
           7 S L32 AND L21
7 S L33 AND L28
L33
L34
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3 S L34 NOT PY>2001

L35